Applicants

Jason Francis Conaty et al. 09/887,880

Serial No. Filed

June 22, 2001

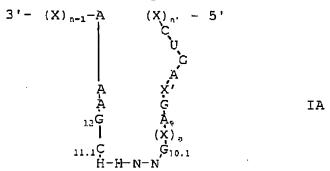
Page 2

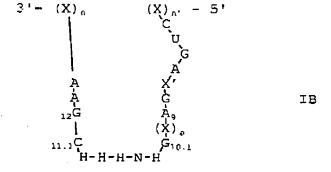
In the Claims

Please cancel claims 25-30 without prejudice to applicants' rights to pursue the subject matter of these claims in this or a related application.

Please amend claims 21 and 31 by replacing all prior versions of the claims pursuant to 37 C.F.R. \$1.121 as modified by 68 Fed. Reg. 38611 (June 30, 2003) as indicated below.

1. (Previously presented) A compound of the formula IA or IB:





wherein each X represents a nucleotide which may be the same or different and may be substituted or modified in its sugar, base or phosphate; and wherein $G_{10.1}$ and $C_{11.1}$ each represent a nucleotide which may be substituted or modified in its sugar (which may be ribose or deoxyribose), base or phosphate;

wherein each of C, G, A and U represents a ribonucleotide

Applicants : Jason Francis Conaty et al.

Serial No. : 09/887,880

Filed : June 22, 2001 Page 3

which may be substituted or modified in its sugar, base or phosphate;

wherein each of $(X)_n$, $(X)_{n-1}-A$ and $(X)_n$, represents an oligonucleotide having a pre-determined sequence which hybridizes with an RNA target sequence to be cleaved, such RNA target sequence not being present within the compound, and each of n and n' represents an integer which defines the number of nucleotides in the oligonucleotide;

wherein X' represents a ribonucleotide selected from C, G, A and U which may be substituted or modified in its sugar, base or phosphate;

wherein a defines the number of nucleotides in $(X)_a$ and may be 0 or 1 and if 0, the A located 5' of $(X)_a$ is bonded to the G located 3' of $(X)_a$;

wherein each solid line represents a chemical linkage providing covalent bonds between the nucleotides located on either side thereof;

wherein each N represents a nucleotide selected from C, G, A and U/T which may be substituted or modified in its sugar (which may be ribose or deoxyribose), base or phosphate and wherein each H represents a nucleotide selected from C, A and U/T, which may be substituted or modified in its sugar (which may be ribose or deoxyribose), base or phosphate; with the proviso that the sequence 5'-NNHH-3' is not UUUU or TTTT, CUCC, AAUU or GGCA.

- 2. (Previously presented) The compound of claim 1, wherein in the formula IB the oligonucleotide $3'-(X)_n-$ is $3'-(X)_{n-1}-A-$.
- 3. (Original) The compound of claim 1, wherein $(X)_a$ is absent.
- (Original) The compound of claim 1, wherein the sum of n+n' is greater than 14.

Applicants : Jason Francis Conaty et al. Serial No. : 09/887,880

Serial No. : 09/887,880 Filed : June 22, 2001 Page 4

5. (Previously presented) The compound of claim 1, wherein the sequence 5'-NNHH-3' is a linker sequence selected from the following classes of linker sequences:

Class I: YRHH, wherein Y is C or U, R is G or A, and H is C, A or U;

Class II: DYHH, wherein D is G, A or U, Y is C or U, and H is C, A or U;

Class III: GHHA, wherein H is C, A or U; and Class IV: WYHH, wherein W is A or U, Y is C or U, and H is C, A or U.

- 6. (Original) The compound of claim 5, wherein the linker sequence is selected from the sequences CGUU, UGUU and UAAC.
- 7. (Original) The compound of claim 5, wherein the linker sequence is a sequence of the class WYHH, wherein W is A or U, Y is C or U, and H is C, A or U.
- 8. (Original) The compound of claim 7, wherein the linker sequence is selected from the sequences ACCC, AUUU, UCCC, AUUC, AUUA, ACAC, AUAA and AUAC.
- 9. (Original) The compound of claim 7, wherein the linker sequence is the sequence UUHH, wherein H is C, A or U.
- 10. (Original) The compound of claim 9, wherein the linker sequence is selected from the sequences UUAC, UUCC, UUUC, UUUA, UUAA and UUAU.
- 11. (Original) The compound of claim 5, wherein the linker sequence is selected from the sequences GUAA and GAUA.

Applicants :

Jason Francis Conaty et al. 09/887,880 Serial No. :

Filed June 22, 2001 Page 5

12. (Previously presented) The compound of claim 1, wherein the sequence 5'-HNHHH-3' in the compound of formula IB is selected from the sequences UCCCA, UCCCC, UCCUA, AAUUU, UUAAA, UUUUA, UGUCC, UGUUA and CACCC.

- 13. (Previously presented) The compound of claim 12, wherein the sequence 5'-HNHHH-3' in the compound of formula IB is selected from the sequences UCCCC, UGUCC and CACCC.
- (Original) The compound of claim 1, wherein each nucleotide 14. in the linker sequence 5'-NNHH-3' or the linker sequence 5-HNHHH-31 is a deoxyribonucleotide.
- 15. (Original) A composition which comprises a compound of claim 1 in association with an acceptable carrier.
- 16. (Original) A composition which comprises a compound of claim 5 in association with an acceptable carrier.
- 17. (Original) An oligonucleotide transfer vector containing a nucleotide sequence which on transcription gives rise to the compound of claim 1 or claim 5.
- 18. (Original) The oligonucleotide transfer vector of claim 17, wherein the transfer vector is a bacterial plasmid, a bacteriophage DNA, a cosmid, or an eukaryotic viral DNA.
- 19. (Original) The oligonucleotide transfer vector of claim 17, wherein the oligonucleotide transfer vector is a plant DNA virus, a geminivirus or an infective phage particle.
- 20. (Original) The oligonucleotide transfer vector of claim 17,

Applicants : Jason Francis Conaty et al.

Serial No. : 09/887,880 Filed : June 22, 2001

Page 6

wherein the oligonucleotide transfer vector is packaged and contains the promoter sequences for RNA polymerase II or RNA polymerase III.

- 21. (Currently Amended) A host cell transformed <u>in vitro</u> by the transfer vector of claim 17.
- 22. (Original) The host cell of claim 21, wherein the host cell is a prokaryotic host cell or an eukaryotic host cell.
- 23. (Original) The prokaryotic host cell of claim 22, wherein the prokaryotic host cell is an *E.coli* host cell.
- 24. (Original) The eukaryotic host cell of claim 22, wherein the eukaryotic host cell is a monkey COS host cell, a Chinese hamster ovary host cell, a mammalian host cell or a plant host cell.

25-30. (Canceled)

- 31. (Currently Amended) A method of cleaving a target mRNA in a host cell <u>in vitro</u> which comprises administering to the host cell an effective amount of a compound of claim 1 or claim 5, or a transfer vector which on transcription expresses a compound of claim 1 or claim 5.
- 32. (Previously presented) The compound of claim 1 or claim 5 which further comprises an antisense nucleic acid which hybridizes with an RNA target sequence.
- 33. (Previously presented) The compound of claim 1 or claim 5 which further comprises at least one additional non-naturally occurring oligonucleotide compound which

Applicants : Jason Francis Conaty et al.

Serial No. : 09/887,880 Filed : June 22, 2001 Page 7

comprises nucleotides whose sequence defines a conserved catalytic region and nucleotides whose sequence hybridizes with a predetermined target sequence.

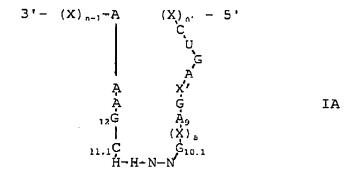
34. (Original) The compound of claim 33, wherein the additional non-naturally occurring oligonucleotide compound is a hammerhead ribozyme, a miniribozyme, a hairpin ribozyme, a hepatitis delta ribozyme, an RNAase P ribozyme, a Group I intron, or a combination thereof.

Jason Francis Conaty et al. 09/887,880 June 22, 2001 Applicants

Serial No. Filed

Page 8

35. (Previously presented) The compound of claim 1 having the formula:



36. (Previously presented) The compound of claim 1 having the formula:

